REMARKS

Reconsideration of this Application is respectfully requested.

Status of the claims

Please cancel claims 27, 35, 42, 58, and 59 without prejudice. Claims 1, 28, 39, 41, 42, 51, 55, 56, and 57 are amended and 61-96 are newly added herein. These changes introduce no new matter, and their entry is respectfully requested.

Upon entry of the foregoing amendments, claims 1-4, 6-28, 30-34, 36, 37, 39, 41, and 43-96 are pending in the application. Claims 2-4, 6-15, 18-26, 31-34, 36, 37, and 43-50 are withdrawn from consideration. Claims 1, 16, 17, 28, 30, 39, 41, and 51-96 are under prosecution.

Based on the above amendments and the following remarks, applicant respectfully requests that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

Claim Amendments

Applicants have amended independent claims 1, 39, 41, and 51 to expedite prosecution of the application. These amendments add no new matter, and their entry is respectfully requested. Amended independent claims 1, 41, and 51 now recite in vitro synthesis systems, kits, and compositions comprising: 1) an extract of E. coli cell having a mutation of a nuclease, in which that E. coli cell does not express Gam; and 2) Gam. Independent claim 39 has also been amended to include 1) an extract of an E. coli cell does not express Gam; 2) at least one energy source; and 3) Gam. Support for these amendments can be found throughout the specification as well as in the claims as originally filed. For example, extracts of E. coli cells having a mutated nuclease gene are disclosed at least in paragraph [0100], and nuclease mutants that do not express Gam are provided in Examples 1 and 8. Gam finds support at least in Examples 4-7.

Newly added dependent claims 61-84 are drawn to nucleases that can be mutated in cells used to make the extract. These claims add no new matter, and find support, for example, in paragraphs [0048] and [0049], as well as in Examples 1 and 8.

Newly added dependent claims 85-96 are drawn to energy sources that can be provided in the claimed compositions. These claims add no new matter, and find support in, for example, paragraphs [0054], [0075], [0076], [0077], [0086], [0087], [0089], and [0090], as well as in Example 9.

Dependent claims 28, 42, 55, 56, and 57 have been amended to conform to the language of the amended independent claims or to clarify claim language. No new matter has been added.

Claims Rejections under 35 U.S.C. §112, First Paragraph, Written Description

The examiner has rejected claims 1, 16, 17, 27, 28, 30, 35, 39, 41, 42, and 51-60 under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one of skill in the art, that the inventors, at the time the application was filed, had possession of the claimed invention.

The Office Action of September 12, 2005 alleges that the specification "fails to teach sufficient structural characteristics of the cells from which the extract is prepared for one of skill in the art to make any species within the scope of the claims. Similarly the genus of recBCD inhibitors encompassed lacks description as the specification fails to teach sufficient structural characteristics of the inhibitor for one of skill in the art to make any species within the scope of the claims" (page 3 of the Office Action, lines 5-12). Applicants point out that these are not criteria for meeting the Written Description requirement of §112, first paragraph, but rather are issues relating to the Enablement requirement. The Written Description requirement of §112 requires that the Applicant:

> . . . convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention, and that the invention, in that context, is whatever is now claimed. The test for sufficiency of support in a parent application is whether the disclosure of the application relied upon "reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter." *Ralston Purina Co. v. Far-Mar-Co., Inc.*, 772 F.2d 1570, 1575, 227 USPQ 177, 179 (Fed. Cir. 1985) (quoting *In re Kaslow*, 707 F.2d 1366, 1375, 217 USPQ 1089, 1096 (Fed. Cir. 1983)).
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> [MPEP 2163.02]

Applicants assert that the Office Action has not presented "a preponderance of evidence why a person skilled in the art would not recognize in an applicant's disclosure a description of the invention defined by the claims. *Wertheim*, 541 F.2d at 263, 191 USPQ at 97." [MPEP 2163.04], with respect to claims 1, 16, 17, 27, 28, 30, 35, 39, 41, 42, and 51-60.

Nevertheless, to expedite prosecution of the application, applicants have amended independent claims 1, 39, 41, and 51 and canceled independent claim 42 and dependent claims 27, 35, 58, and 59. As amended, independent claims 1, 41, and 51 recite an in vitro synthesis system, a kit, and a composition, respectively, comprising 1) an extract from an E. coli cell having a mutation that results in reduced activity of a nuclease, in which the E. coli cell does not express Gam; and 2) Gam. Independent claim 39 as amended recites a composition that includes 1) an extract from an E. coli cell that does not express Gam; 2) at least one energy source; and 3) Gam. Applicants contend that these aspects of the invention are disclosed in the application in a manner to convey to one skilled in the art that the inventors had possession of the claimed invention. An extract from an E. coli cell having a mutation that results in reduced activity of a nuclease is disclosed throughout the application, for example, at least in paragraphs [0038], [0039], [0048] and [0049], [0107]. Such mutant strains of E. coli that do not express Gam are provided, for example, in Examples 1 and 8. Gam is disclosed, for example, in Examples 2-7 of the specification. Applicants therefore contend that the Written Description requirement of §112 is met for independent claims 1, 39, 41, and 51, and to dependent claims 16, 17, 28, 30, and 55 that depend from claim 1, dependent claim 56 that depends from claim 39, dependent claim 57 that depends from claim 41, and dependent claims 52-54 and 60 that

depend from claim 51. Claims 27, 35, 42, 58, and 59 are canceled herein, and therefore their rejection is rendered moot. Applicants therefore respectfully request that the rejection of claims 1, 16, 17, 27, 28, 30, 35, 39, 41, 42, and 51-60 under the Written Description requirement of 35 U.S.C. §112, first paragraph, be removed.

Claims Rejections under 35 U.S.C. §112, First Paragraph, Enablement

The examiner has rejected claims 1, 16, 17, 27, 28, 30, 35, 39, 41, 42, and 51-60 under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one of skill in the art to make and use the invention as claimed.

Applicants do not agree that the subject matter of claims 1, 16, 17, 27, 28, 30, 35, 39, 41, 42, and 51-60 is not enabled by the specification. Nevertheless, to expedite allowance of claims, Applicants have canceled claims 27, 35, 42, 58, and 59, and amended independent claims 1, 41, and 51 to recite in vitro synthesis system, a kit, and a composition, respectively, comprising 1) an extract from an E. coli cell having a mutation that results in reduced activity of a nuclease, in which the E. coli cell does not express Gam; and 2) Gam. Independent claim 39 as amended recites a composition that includes 1) an extract from an E. coli cell that does not express Gam; 2) at least one energy source; and 3) Gam. Applicants appreciate the Examiner's statement in the Office Action of September 12, 2005, that the specification is "enabling for in vitro transcription and/or translation systems comprising an extract of E. coli having one or more nuclease genes mutated to reduce the activity of the encoded nuclease and a λ Gam protein or kits therefore . .". Applicants

therefore assert that in accordance with the Office Action of September 12, 2005, independent claims 1, 41, and 51 as amended are enabled under 35 U.S.C. §112, first paragraph. Claims 16, 17, 28, 30, and 55 that depend from claim 1; claim 57 that depends from claim 41; and claims 52-54 and 60 that depend from claim 51 are also enabled under 35 U.S.C. §112, first paragraph. Applicants assert that these aspects of the invention are disclosed throughout the application, and particularly in Example 7, in a manner that would enable one skilled in the art to make and use the claimed composition. Claim 56, that depends from claim 39, is also fully enabled by the specification, including, for example, Example 9. Claims 27, 35, 42, 58, and 59 are canceled herein, and therefore their rejection is rendered moot. Applicants therefore respectfully request that the rejection of claims 1, 16, 17, 27, 28, 30, 35, 39, 41, 42, and 51-60 for lack of Enablement under 35 U.S.C. §112, first paragraph, be removed.

Claims Rejections under 35 U.S.C. §103(b), Pratt and Yu

The Examiner has rejected claims 1, 16, 17, 27, 28, 30, 35, 39, 41, 42, and 51-60 as being obvious under 35 U.S.C. §103(a) over Pratt in view of Yu et al. Applicants do not agree that Pratt or Yu, alone or in combination, render the claims obvious. To expedite allowance of claims, however, applicants have amended independent claims 1, 39, 41, and 51 and canceled claims 27, 35, 42, 58, and 59. Amended claims 1, 41, and 51 now recite: 1) at least one extract from an E. coli cell that does not express Gam, in which the E. coli cell is mutated to reduce the activity of at least one nuclease; and Gam. Independent claim 39 as amended recites: 1) at least one extract from an E. coli

cell that does not express Gam; 2) least one energy source; and 3)Gam.

The MPEP states that to establish a prima facie case of obviousness there must be some suggestion or motivation in the prior art to make the claimed invention, there must be a reasonable expectation of success, and the prior art reference must teach or suggest all of the claim limitations. MPEP § 2142; In re Vaeck, 947 F.2d 488, 20 USPQ2d, 1438 (Fed. Cir. 1991). The reference teachings must be sufficient for one of ordinary skill in the relevant art having the reference before him to make the proposed substitution, combination, or other modification. In re Linter, 458 F.2d 1013, 1016, 173 USPQ 560, 562 (CCPA 1972). MPEP 2143.01. Applicants assert that the requirements of a rejection under 35 U.S.C. §103(b) are not been met for at least the following reasons.

The references fail to provide a suggestion or motivation for making the claimed invention. The Office Action states "Yu et al. clearly discloses that the production of the Gam protein within a genetic background including wild type production of the E. coli recBCD exonuclease can be used as a substitute for a mutant strain lacking the nuclease". Applicants respectfully point out that "production of the Gam protein within a genetic background including wild type production of the E. coli recBCD exonuclease. . ." is not recited in the claims as amended. Rather, the claims recite compositions that include an E. coli extract, and Gam, in which the Gam is not expressed by the E. coli cell used to make the extract. The cited references provide no suggestion or motivation for this combination. Yu et al. is concerned with recombination into the E. coli genome and does not refer in vitro synthesis systems or cell

extracts, and certainly does not disclose, suggest, or motivate combining Gam protein with an extract of a cell that does not express Gam. Pratt, in discussing the use of linear DNA templates in E. coli in vitro synthesis systems also does not anywhere suggest or motivate the use of an inhibitor of recB. In fact, Pratt suggests an alternative strategy, the use of a recB mutant as a source of extracts for in vitro synthesis. As disclosed in Pratt, however, this system has an undesired consequence of resulting in undegraded bacterial DNA in the cell extract that leads to background transcription/translation in the synthesis system. Pratt provides a solution to this: The system of Gold and Schweiger (see section 5.1.2 of Pratt). The method of Gold and Schweiger, as related by Pratt, includes the use of a DEAE cellulose column to remove unwanted nucleic acid template from the extract prior to use in in vitro synthesis reactions: "Extracts prepared from recB strains fractionated in this way have been used successfully by a number of workers to study proteins encoded by specific restriction endonuclease-generated fragments." (Pratt, page 202). Thus, Pratt never suggests use of a recBCD inhibitor. To the contrary, Pratt suggests used of a recB mutant (obviating the need for an inhibitor, as no activity is present) combined with chromatography to solve the problem of residual E. coli DNA present in the extract.

The present invention uses completely different methodology not suggested or motivated by the references, namely, use of a protein inhibitor (Gam) that is not expressed by cells used to make the extract for synthesis, in which the protein can eliminate unwanted activity of an enzyme (recBCD) at the appropriate time and in a titratable manner. The use of Gam, as opposed to an engineered cell expressing Gam, allows wild-type recBCD to be active during growth of the cell and processing of the extract, and subsequently allows for the inhibition of recBCD activity during in vitro synthesis

reactions. This is not possible using the system of Pratt or the system of Yu, nor by any combination of features disclosed by these references.

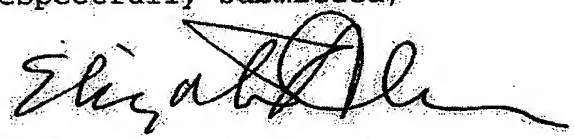
Thus, the references do not disclose each and every element of rejected independent claims 1, 39, 41, and 51 as amended. Further, here is no suggestion in the references for making the invention as set forth in independent claims 1, 39, 41, and 51 as amended. Claims 27, 35, 42, 58, and 59 are canceled herein, and thus their rejection is rendered moot. Claims 16, 17, 28, 30, and 55 depend from claim 1; claim 56 depends from claim 39; claim 57 that depends from claim 41; and claims 52-54 and 60 depend from claim 51. These claims are patentable under 35 U.S.C. §103(b) for the same reasons independent claims 1, 39, 41, and 51 are patentable. Applicants therefore respectfully request that the rejection of claims 1, 16, 17, 27, 28, 30, 35, 39, 41, 42, and 51-60 under 35 U.S.C. §103(a) be removed.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicant therefore respectfully requests that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicant believes that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,



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